REMARKS

I. Amendments

By this amendment, new claims 30-32 have been added.

This amendment adds no new matter to the specification. Support for this amendment is found in the specification and claims as filed.

No amendment of inventorship is necessitated by this amendment.

II. Discussion of the Advisory Action

In the Advisory Action, the Examiner indicated that Applicants' response filed January 30, 2003 would not be entered because it raised new issues. However, the Examiner's comments also indicated that new claims 30-32 would be withdrawn from consideration. Applicants do not understand what the new issues are, if claim 30-32 were actually to be withdrawn.

Moreover, no comment was provided in the Advisory Action as to the Applicants well-reasoned arguments to overcome the outstanding rejections.

Applicants respectfully request the Examiner's thorough consideration of the present case; with careful attention to each of Applicants' salient points. Applicants make this request out of a concern that the Examiner has not carefully considered their case in the past, as evidenced by the Examiner's lack of responsiveness to Applicants' arguments thusfar.

As a specific example, Applicants have indicated that the Shimizu reference is not proper art in their response dated January 30, 2003. They made the same argument in the submission dated July 9, 2002. To date, the Examiner has neglected to even respond to this aspect of Applicants' arguments.

If the Examiner wishes to maintain any of her rejections after reviewing this response, Applicants respectfully request that Examiner provide a separate comment individually addressing each point discussed by Applicants; so that the case can be made in order for an Appeal.

III. Discussion of the Rejection under 35 U.S.C. Sec. 103(a) over Shimizu *et al.*

Claims 20, 21, 23-26, 28 and 29 have been newly rejected under 35 U.S.C. Sec. 103(a) as unpatentable over Shimizu *et al.*, U.S. Patent No. 6,299,904. Applicants respectfully traverse the rejection as the cited reference is not proper art.

Applicants provided a Certified Copy of the translation of the Japanese priority document with their last response, to ensure that priority had been perfected for the present application. Receipt of that document was acknowledged, but in fact the Certified Copy of the Priority document was already indicated as acknowledged in the Office Action Summaries of June 13, 2000 and May 9, 2001.

Applicants' position is that since the present application has priority, the cited reference is not art and the rejection should be withdrawn. Unfortunately, the Examiner neglected to address this point in the latest Office Action.

For the reason provided above, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. Sec. 103(a) rejection over Shimizu *et al.*

IV. Discussion of the Previous Rejection under 35 U.S.C. Sec. 103(a) over Ohno *et al.*

In the Office Action dated April 12, 2002, claims 20, 21, 23-26, 28 and 29 had been rejected under 35 U.S.C. Sec. 103(a) as unpatentable over Ohno *et al.*, U.S. Patent No. 5,958,453. Since this rejection is not repeated in the present Office Action dated October 9, 2002, Applicants presume the rejection has been overcome.

In confirmation, Applicants respectfully request that the Examiner state for the record that the previous rejection under Sec. 103(a) rejection over Ohno *et al.* has been withdrawn.

V. Discussion of the Rejection under 35 U.S.C. Sec. 103(a) over Ohno *et al.* in view of Shimizu *et al.*

Claims 21, 21, 23-26, 28 and 29 have been rejected under 35 U.S.C. Sec. 103(a) as unpatentable over Ohno *et al.*, U.S. Patent No. 5,958,453 in view of Shimizu *et al.*, U.S. Patent No. 6,299,904. Applicants respectfully traverse the rejection.

As stated in Sec. III above, Applicants do not believe the '904 patent is citable against them, in view of the priority of their application. As above, this point was presented in Applicants' previous response but went unaddressed in the present Office Action.

Since the '904 reference is not proper art, the teachings of the '904 reference cannot be combined with the teachings of the '453 reference to obtain the aspects of the invention set forth in the pending claims.

Therefore, Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 103(a) over Ohno *et al.* in view of Shimizu *et al.*

VI. Discussion of the Rejection under 35 U.S.C. Sec. 103(a) over Ohno *et al.* in view of Shashoua *et al.*

Claims 20, 21, 23-26, 28 and 29 have been rejected under 35 U.S.C. Sec. 103(a) as obvious over the Ohno *et al.*, U.S. Patent No. 5,958,453 in view of Shashoua *et al.*, U.S. Patent No. 5,795,909. For a number of reasons, the combination of the cited references does not teach or suggest the Applicants' invention as set forth in the pending claims. Each reason will be discussed in the following paragraphs. Applicants invite the Examiner to address each aspect of Applicants' reasons for patentability separately, should she choose to maintain the rejection.

Reason 1: Cited Art Teaches Away From the Invention

The '357 reference does not teach that L-HPC is a choice for a solid formulation which disintegrates quickly. In the '357 reference, comparative examples are presented, wherein formulations with and without L-HPC are evaluated in terms of dissolution time. In every instance, the formulations including L-HPC demonstrate significantly longer dissolution times.

Specifically, in Example 4, without L-HPC a dissolution time of 45 seconds is recorded, whereas with L-HPC a buccal dissolution time more than twice slower (105 seconds) is recorded. In Example 5, without L-HPC a dissolution time of 28 seconds is recorded, whereas with L-HPC a buccal dissolution time which is three times slower (85 seconds) is recorded.

No one skilled in the art would have been motivated to add L-HPC to a formulation to increase dissolution time; and certainly no one skilled in the art would have expected that a specific L-HPC could be added to a formulation in order to achieve a buccal dissolution time of 5 to 50 seconds, as specified in independent method claims 20 and 21, in light of the

experimental results presented. Therefore, the '357 reference teaches away from the present invention.

The deficiencies of the '357 reference are not cured by the '909 reference in this respect.

Despite these results, Applicants were able to actually create a formulation wherein L-HPC is added and dissolution time is favorably affected. How is this possible, given the '357 reference? The answer is found in the paragraphs under Reason 2.

Reason 2: Cited Art Does Not Teach the Present L-HPC Component

The '357 reference does not teach or suggest the presently specified L-HPC merely because an L-HPC is added to certain formulations. The experimental evidence of the '357 reference proves this point, as the results which the Applicants set forth in the present application could not have been achieved before because the L-HPC now recited was not available at the time of the '357 reference. Had it been available, desirable dissolution times could have readily been obtained by the authors of the '357 reference. They were not because the L-HPC component of the present formulation was not available.

Documents to prove that low-substituted hydroxypropylcellulose having 5% to less than 7% was not available at the time of the '357 reference were previously submitted on January 15, 2002. A catalogue for the appropriate time period from Shin-Etsu Corp. (the supplier of L-HPC) shows that the presently claimed L-HPC was not sold. Additionally, a Declaration from a Shin-Etsu employee states that L-HPC having the low hydroxypropylcellulose content presently claimed was unavailable. Further evidence is provided by an author of the '357 reference (Mr. Ohno) who states that the L-HPC used in the experiments of the reference had a hydroxypropylcellulose content no lower than 10%; and moreover that there would have been no motivation to use L-HPC to improve oral formulations given the poor results which he reported.

The Examiner has stated previously that all of this evidence is not convincing because no surprising results are obtained. According to the Examiner, since the '357 reference indicates that formulations can be made having buccal dissolution times of 0.1 –1 minute; and the reference shows formulations including L-HPC; that the Applicants' invention as set forth in the pending claims is obvious. However, the Examiner has merely gleaned a point or two from this reference and quickly arrived at an erroneous assumption. One skilled in the art would not have interpreted the reference in this way, but rather would have taken the reference as a whole, and learned from the presented examples that L-HPC could **NOT** be used to achieve even the

broadest stated range of buccal dissolution times (up to a minute). So the Examiner's statement that no unexpected results were obtained is just plain wrong.

The Examiner has ignored the principle that the cited art should be considered in its entirety. It has been stated that "[i]t is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art" in *In re Wesslau*, 353 F.2d 238, 241. This statement characterizes what the Examiner has done in this instance to stretch the '357 reference such that it covers the present invention. Not only do the Applicants assert that the Examiner's characterization of what the '357 reference teaches those skilled in the art is wrong; but also they've provided a Declaration from Mr. Ohno (one actually skilled in the art) which verifies their point.

Put another way, the '357 reference does not enable what the Examiner believes it discloses; i.e. – that L-HPC can be put into a formulation to achieve buccal dissolution time of 0.1 – 1.0 minutes.

The deficiencies of the '357 reference are not cured by the '909 reference in this respect.

Reason 3: No Incentive to Combine the Two Cited References

In addition to the points made above, Applicants also continue to assert that there is no motivation to combine the two cited references.

The Examiner has indicated that the '909 reference has been cited because it recites the active ingredient and a carrier as components of a pharmaceutical formulation, and also indicates that the formulation can be in tablet form. Although the active agent and tablet formulation are briefly mentioned, Applicants assert that the '909 reference would not have been consulted by one skilled in the art seeking to create a rapidly disintegrable solid preparation.

This reference is directed to conjugates useful for treating cell proliferative disorders, wherein an active agent is combined with another chemical compound. Examples of test solutions are provided; and it is indicated that intravenous administration of the conjugates are preferable in the reference. One preparing to create a novel tablet or solid formulation would not have chosen to review and incorporate the teachings from a reference disclosing IV solutions. So there is no reason to combine the '909 reference with the '357 reference.

The Examiner previously indicated that since the '909 reference includes lansoprazole, and the '357 reference is not limited as to pharmaceutically active ingredients, but includes gastrointestinal function conditioning agents, that the two references can reasonably be combined. However, this statement can only be made in blind ignorance of the entirety of the '909 reference, wherein active agents are conjugated to another compound and the conjugate is put into a solution. A solution for IV use does not to have a property of rapid disintegrability; as it is already dissolved. So Applicants assert that although the Examiner's reason for combining the two references appears logical to the Examiner on paper, those skilled in the art would not have seen or made any connection between the two references.

Therefore, Applicants continue to assert that the two references would not have been combined by those skilled in the art; and moreover that the Examiner here again has merely gleaned a word or two from a reference without considering the teaching as a whole prior to making a broad characterization of the reference.

Therefore, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. Sec. 103(a) over Ohno *et al.*, U.S. Patent No. 5,958,453 in view of Shashoua *et al.*, U.S. Patent No. 5,795,909.

VII. Discussion of New Claims 30-32

By this amendment, new independent claims 30 and 32 have been added, and related dependent claims 31 has been added. These claims add no new matter to the specification.

In the new independent claims, tablets which have no roughness and which are improved in chalky taste are recited. These virtues are imparted by the use of the recited specified low-substituted hydroxypropylcellulose (L-HPC).

This specific type of L-HPC was not sold when the invention disclosed in the '357 reference was made, as Applicants have explained in their response and accompanying supporting documents dated January 15, 2002.

Moreover, the '357 reference does not suggest that use of the specified L-HPC can lead to tablets having the special and advantageous characteristics of not being rough and not tasting so chalky. That is so because the L-HPC's available at the time of the invention of the '357 reference could not achieve this result.

Applicants claim tablets having a special ingredient (a specific type of L-HPC) which leads to an advantageous result (no roughness, less chalky taste). The '357 reference does not

teach or suggest the specified L-HPC and also does not teach or suggest the characteristic imparted, since the L-HPC's of that time could not impart that characteristic.

The deficiencies of the '357 reference are not cured by the '909 reference, which the Examiner asserts is only cited to provide the active ingredient in a carrier.

Therefore, Applicants submit that claims 30-32 are patentable.

VIII. Discussion of Withdrawal of New Claims 30-32

In the Advisory Action, the Examiner indicated that claims 30-32 would be withdrawn, as directed to a non-elected invention. However, originally filed dependent claim 3 recited tablets, while originally filed dependent claim 13 recited fine granules. A restriction requirement was not imposed upon the original claims. New independent claims 30 and 32 are directed to tablets comprising fine granules.

Applicants do not believe that claims 30-32 should be withdrawn. Applicants respectfully request the Examiner's reconsideration of withdrawal of these claims, in light of the claims as originally filed.

IX. Conclusion

Reconsideration of the claims in view of the arguments made above is solicited. Should the Examiner believe that a conference with Applicants' attorney would advance prosecution of this application, she is respectfully requested to call Applicants' attorney.

Respectfully submitted,

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